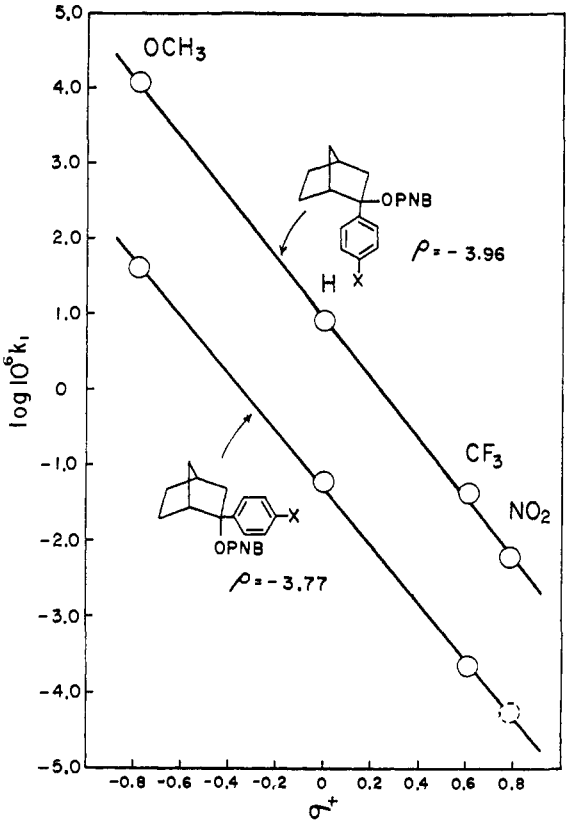

Figure 1. Correlation with σ^+ constants of the rates of solvolysis in 80% aqueous acetone at 25° of 2-aryl-*exo*- and -*endo*-norbornyl *p*-nitrobenzoates.

solvolysis rates in 80% acetone. The results are summarized in Table I. The data give excellent σ^+ plots (Figure 1).

We also carried out trapping experiments on the corresponding chlorides.[8] As indicated by the data in Table II, all compounds consistently gave predominant *exo* attack of borohydride.

Table II. Trapping of the Carbonium Ion by Sodium Borohydride in the Solvolysis of the Substituted 2-Aryl-*exo*-norbornyl Chlorides in 70% Diglyme at 25°

Substituent	Yield of 2-arylnorbornane, %[a]	2-Arylnorbornane, %[b] *exo*-H	*endo*-H
p-CH_3O	68	≥98	≤2
p-H	82	≥98	≤2
p-CF_3[c]	32	≥97	≤3
p-NO_2	59	≥97	≤3

[a] Glpc analysis. [b] Analysis for isomers by pmr. [c] Mp 51.0–51.5°.

It is evident that there is no observable increase in the *exo–endo* rate ratios as electron-withdrawing substituents are introduced into the aromatic ring over the range examined. Consequently, it is quite clear that σ participation cannot be a significant factor in the high *exo*:*endo* rate ratios and the predominant *exo* substitution of these derivatives.

Conflicting opinions have been expressed as to whether the 2-methyl-2-norbornyl cation is classical[9] or nonclassical.[10] However, the reactivity of 2-*p*-nitrophenyl-2-norbornyl is practically identical with that of 2-methyl-2-norbornyl.[7] Electron demand at the electron-deficient center of these two systems should be essentially identical. Since the present results support the conclusion that σ participation is not a factor in the 2-*p*-nitrophenyl derivative, it cannot be a factor in the 2-methyl structure, supporting the view that the 2-methyl-2-norbornyl cation must be essentially classical.[9]

The present data do not permit a definitive answer to the question of whether σ participation is present in norbornyl itself. Even with the least reactive derivative we have studied, 2-*p*-nitrophenyl-2-norbornyl, we have progressed only 60% of the reactivity range from 2-*p*-anisyl-2-norbornyl to 2-norbornyl.[7] However, the present results clearly imply that if such σ participation is present, it cannot be large. This conclusion is based on the observation that the *exo*:*endo* rate ratios in the present 2-aryl derivatives are of the same order of magnitude as that observed in norbornyl itself, and equilibration studies[11] do not permit any large contribution from the differences in ground-state energies.

It follows that even in norbornyl, a major if not the only important contribution to the *exo–endo* rate ratio must be a blend of steric[4] and torsional[5] effects.

(8) H. M. Bell and H. C. Brown, *J. Am. Chem. Soc.*, **88**, 1473 (1966).
(9) C. A. Bunton, "Nucleophilic Substitution at a Saturated Carbon Atom," Elsevier Publishing Co., New York, N. Y., 1963, p 62.
(10) S. Winstein, *J. Am. Chem. Soc.*, **87**, 381 (1965).
(11) M. H. Rei and H. C. Brown, *ibid.*, **88**, 5335 (1966).
(12) Research assistant on grants (G 19878 and GP 6492X) supported by the National Science Foundation.

Ken'ichi Takeuchi,[12] Herbert C. Brown
Richard B. Wetherill Laboratory
Purdue University, Lafayette Indiana 47907
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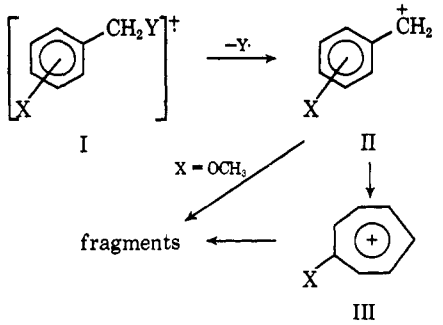
Occurrence and Timing of the Rearrangement of Benzyl Ions to Tropylium Ions in the Mass Spectra of Substituted Benzyl Phenyl Ethers

Sir:

Among the most challenging current problems in mass spectrometry is the assignment of ion structures and the detailed elucidation of fragmentation pathways. We report here application of the elegant techniques of kinetic substituent effects[1-3] and metastable ion characteristics[4,5] recently developed by McLafferty and coworkers to the general question of ion structure in the decomposition of substituted benzyl derivatives I. The results obtained with substituted benzyl phenyl ethers (I, Y = OC_6H_5) suggest that in the ionizing electron energy range 20–70 eV benzyl-type ions II can be precursors to rearranged tropylium ions III and are interpreted most simply in terms of the following stepwise scheme.

(1) M. M. Bursey and F. W. McLafferty, *J. Am. Chem. Soc.*, **88**, 29 (1966).
(2) M. M. Bursey and F. W. McLafferty, *ibid.*, **89**, 1 (1967).
(3) (a) F. W. McLafferty and T. Wachs, *ibid.*, **89**, 5043 (1967), and previous papers in this series. (b) For a recent review, see M. M. Bursey, *Org. Mass Spectrom.*, 1, 31 (1968).
(4) T. W. Shannon and F. W. McLafferty, *J. Am. Chem. Soc.*, **88**, 5021 (1966).
(5) W. T. Pike and F. W. McLafferty, *ibid.*, **89**, 5954 (1967), and previous papers in this series.



Meyerson and coworkers[6] have shown by isotope labeling that decomposing ions of formula $C_6H_5CH_2^+$ in the mass spectra of toluene and other benzyl derivatives are best represented by the symmetrical tropylium ion III, X = H. It has also been demonstrated[7] by appearance potential measurements that nondecomposing substituted ions of formula $XC_6H_4CH_2^+$ at threshold again have tropylium ion structures III when X = *m*- and *p*-CH_3, -F, or -OH (from I, Y = halogen), but benzyl structures II when X = *m*- and *p*-OCH_3. These data, however, provide no information concerning the structure(s) of nondecomposing $XC_6H_4CH_2^+$ ions above threshold, *i.e.*, those actually collected and measured, and the possibility remained that higher energy molecular ions of certain benzyl compounds[8] might not generate tropylium ions directly.

In order to probe the structure of $XC_6H_4CH_2^+$ ions in the transition state in which they are formed, we have studied the kinetics of decomposition of a series of substituted benzyl phenyl ethers (I, Y = OC_6H_5). At both 70 and 20 eV (nominally), over 90% of the total ion current is carried by ions I and $XC_6H_4CH_2^+$. Thus despite substituent retention in the daughter ion,[2] an excellent Hammett plot is obtained at either electron energy (Figure 1, 70 eV, $\rho = -0.76$) when relative rates are correlated with σ^+ constants.[10] Attempted correlation with σ values affords a markedly curved line.

The linear relationship suggests that, as with the $XC_6H_4CO^+$ ions from substituted acetophenones and benzophenones,[1] the $XC_6H_4CH_2^+$ ions are not formed in any excited state. The observed substituent effects also indicate that, in the transition state for the cleavage of I → $XC_6H_4CH_2^+$, the potential daughter ion apparently does not have the symmetry of a tropylium structure and that decomposing molecular ions I (Y = OC_6H_5) are not rearranged before cleavage.[11] Thus all isomeric pairs of *meta*- and *para*-substituted benzyl phenyl ethers gave different rates,[13] demonstrating retention of the integrity of the benzene ring and of substituent position.

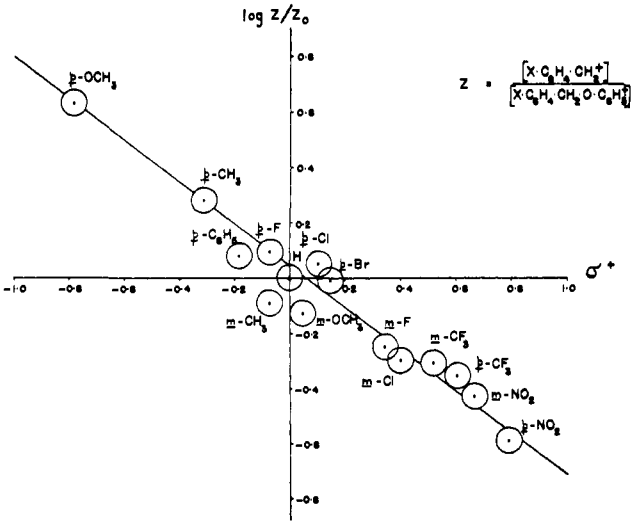


Figure 1. Correlation of the intensities of the $XC_6H_4CH_2^+$ ion in the 70-eV mass spectra of substituted benzyl phenyl ethers. Slope = −0.76.

At 70 eV slight further decomposition of the $XC_6H_4CH_2^+$ ions occurs, and metastable ion characteristics[4,5] were recorded for these transitions (Table I).

Table I. Metastable Ion Abundance Data for the Reaction $XC_6H_4CH_2OC_6H_5 \cdot^+ \rightarrow XC_6H_4CH_2^+$

X	Transition	Metastable	$\frac{[\text{metastable}]}{[XC_6H_4CH_2^+]} \times 10^3$ *m*-X	*p*-X
NO_2	136 → 90	59.6	1.2	1.0
CF_3	159 → 109	74.7	0.65	0.61
	159 → 139	121.5	0.35	0.31
Cl	125 → 89	63.4	0.40	0.28
	125 → 99	78.4	0.14	0.12
	127 → 101	80.3	0.17	0.15
F	109 → 83	63.2	0.35	0.36
CH_3	105 → 77	56.5	0.22	0.18
	105 → 78	57.9	0.16	0.14
	105 → 79	59.4	0.79	0.70
OCH_3	121 → 77	49.0[a]	0.27	0.14

[a] A further metastable peak at *m/e* 68.3 probably arises from both 121 → 91 and 214 → 121.

The effectively constant ratio of metastable ion intensity to precursor ion intensity (columns 4 and 5 of Table I) for all substituents except X = OCH_3 indicates that, at this stage in the fragmentation, substituent positional identity has been lost, and that the transition states for decomposing $XC_6H_4CH_2^+$ ions are identical for each substituent (except methoxy).

For endothermic unimolecular decompositions of gaseous ions, a resemblance between transition state and reaction product is to be expected.[14] Thus although previous evidence for both decomposing[6] (at 70 eV) and nondecomposing[7] (at threshold) $XC_6H_4CH_2^+$ ions in the spectra of substituted benzyl compounds was in favor of tropylium structures III (except

(6) H. M. Grubb and S. Meyerson in "Mass Spectrometry of Organic Ions," F. W. McLafferty, Ed., Academic Press Inc., New York, N. Y., 1963, Chapter 10, and references cited therein.

(7) J. M. S. Tait, T. W. Shannon, and A. G. Harrison, *J. Am. Chem. Soc.*, **84**, 4(1962).

(8) The substituted benzyl phenyl ether system was chosen to provide an extremely labile leaving group, since the analogous processes in toluene[6] (M − H) and ethyltoluenes[9] (M − CH_3) are known to be preceded by rearrangement of the molecular ion, presumably to an ionized cycloheptatriene species.

(9) F. Meyer and A. G. Harrison, *J. Am. Chem. Soc.*, **86**, 4757 (1964).

(10) H. C. Brown and Y. Okamoto, *ibid.*, 80, 4979 (1958).

(11) In a series of *meta*- and *para*-substituted toluenes, where rearrangement prior to cleavage has been clearly demonstrated in the parent compound,[6] we find[12] identical rates for the M − H process for each *meta* and *para* isomer pair, and no correlation with σ or σ^+.

(12) P. Brown, unpublished results.

(13) Alternatively, transition states of the same energy and molecular ions of different energy for each *meta*- and *para*-substituted pair might produce the observed substituent effects. Methods for distinguishing these possibilities are under active investigation.

(14) G. S. Hammond, *J. Am. Chem. Soc.*, 77, 334 (1955).

where X = OCH_3), the present results at 20–70 eV[15,18] can be interpreted most simply in terms of the initial formation of benzyl ions II from unrearranged molecular ions I, followed by rearrangement of II to tropylium ions III (except where X = OCH_3) prior to further fragmentation. The anomalous behavior of methoxy substituents has been noted before,[6,7] and our metastable data (Table I) are in agreement with the proposal[7] that $CH_3OC_6H_4CH_2^+$ ions have different (probably benzylic) structures (II) when derived from isomeric precursors I (X = *m*- and *p*-OCH_3).

Acknowledgment. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. Purchase of the Atlas CH4B mass spectrometer was made possible through Grant No. GB-4939 from the National Science Foundation.

(15) At lower electron energies, relative ion abundances are affected by the proximity of the appearance potential of the product ion.[16,17]

(16) F. W. McLafferty and M. M. Bursey, *J. Org. Chem.*, **33**, 124 (1968).

(17) See ref 3b.

(18) Mass spectra were secured using an Atlas CH4B mass spectrometer equipped with a molecular beam inlet system,[19] operating under the following conditions: probe at room temperature, source at 210°, filament current 3–8 μA. All reported ion abundance measurements were made at least in duplicate.

(19) C. Brunnée, 14th Annual Conference on Mass Spectrometry, ASTM Committee E-14, Dallas, Texas, 1966, p 410.

Peter Brown

Department of Chemistry, Arizona State University
Tempe, Arizona 85281

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A Reagent for Peptide Synthesis. Copoly(ethylene-N-hydroxymaleimide)

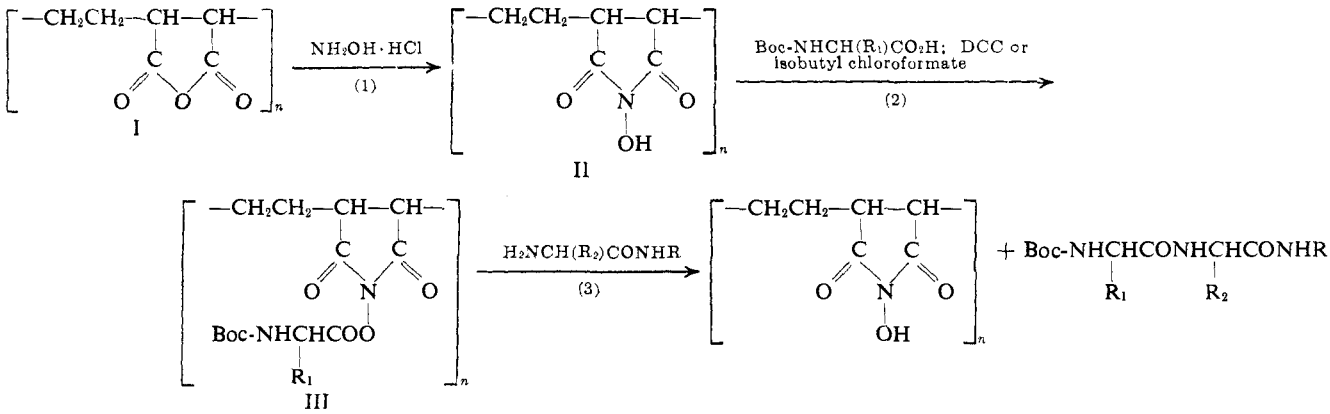
Sir:

The adaptability of reactions involving aminolysis of *t*-butyloxycarbonyl- (Boc-) amino acid N-hydroxysuccinimide (NHS) esters[1] to rapid work-up procedures in peptide synthesis has been recently demonstrated.[2] The use of polymers either as support systems[3] or as reagents[4] in stepwise syntheses of several peptides has been described. We report here a way to use NHS esters as polymeric reagents by (1) the synthesis of copoly(ethylene-N-hydroxymaleimide) (II) and its Boc-amino acid ester derivatives (III) and (2) the application of this polymeric form of NHS-active esters as a reagent in peptide synthesis.

The polymeric NHS (II) was prepared by condensing copoly(ethylenemaleic anhydride) (I) (Monsanto DX 840, 1 equiv) with hydroxylamine hydrochloride (4 equiv) in dimethylformamide (DMF) and distilling the solvent until the boiling point reached *ca.* 153° (Chart I, reaction 1). The exothermic reaction led to II in nearly quantitative yields as a buff-colored powder which was characterized by elemental analysis (*Anal.* Calcd for $C_6H_7O_3N$: C, 51.1; H, 5.0; N, 9.9. Found: C, 51.5; H, 5.7; N, 9.6) and by the characteristic infrared bands of the N-hydroxysuccinimide moiety (1780 (m), 1715 cm^{-1} (s); film cast from DMF). Polymer II was soluble in DMF and dimethyl sulfoxide and insoluble in H_2O, MeOH, EtOH, 2-PrOH, dimethoxyethane (DME), and acetonitrile.

Polymeric NHS esters of Boc-α-amino derivatives[5] of alanine, phenylalanine, O-benzylserine, threonine, β-benzylaspartic acid, methionine, *im*-benzylhistidine, ε-carbobenzyloxylysine, γ-benzylglutamic acid, nitroarginine, and leucine were synthesized in yields of *ca.* 70% either by the mixed anhydride[6] or dicyclohexylcarbodiimide (DCC)[1] methods (Chart I, reaction 2) using DMF as solvent. Use of equimolar quantities of all reactants usually resulted in 90–100% Boc-amino acid substitution of all NHS sites in polymer II. The extent of substitution on the polymer was estimated by amino acid analysis,[7] the characteristic infrared bands of the Boc-amino acid NHS ester moiety (1820 (w), 1740 cm^{-1} (s); films cast from DMF), and by subsequent test peptide coupling reactions. Amino acid substitution was varied (2–100%) by appropriate adjustment of the Boc-amino acid:polymer II molar ratio.

Chart I. Preparation and Reactions of Copoly(ethylene-N-hydroxymaleimide) in Peptide Synthesis



Use of polymeric NHS esters (III) as intermediates in syntheses of peptides listed in Table I was made in

(1) G. W. Anderson, J. E. Zimmerman, and F. M. Callahan, *J. Am. Chem. Soc.*, **86**, 1839 (1964).

(2) D. A. Laufer and E. R. Blout, *ibid.*, **89**, 1246 (1967).

(3) R. B. Merrifield, *ibid.*, 85, 2149 (1963); *Biochemistry*, **3**, 1385 (1964); *J. Org. Chem.*, 29, 3100 (1964); G. R. Marshall and R. B. Merrifield, *Biochemistry*, 4, 2394 (1965); R. B. Merrifield, *Recent Progr. Hormone Res.*, **23**, 451 (1967), and references cited therein; M. M. Shemyakin, Yu. A. Ovchinikov, A. A. Kiryushkin, and I. V. Kozhevnikova, *Tetrahedron Letters*, 2323 (1965).

(4) M. Fridkin, A. Patchornik, and E. Katchalski, *J. Am. Chem. Soc.*, 87, 4646 (1965); **88**, 3164 (1966); T. Wieland and C. Birr, *Angew. Chem. Intern. Ed. Engl.*, **5**, 310 (1966); *Chimia* (Aarau), 21, 581 (1967).

(5) Boc-L-amino acids were purchased from Cyclo Chemical Corp. The alanine and methionine derivatives were once crystallized before use.

(6) G. W. Anderson, F. M. Callahan, and J. E. Zimmerman, *J. Am. Chem. Soc.*, **89**, 178 (1967).

(7) Amino acid analyses of acid-hydrolyzed peptides were carried out with the Beckman-Spinco amino acid analyzer.